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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,142	02/05/2002	Nicholas Maughan Clayton	PG3749USW	7895

23347 7590 10/02/2003

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EXAMINER	
BAHAR, MOJDEH	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 10/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/049,142	CLAYTON ET AL.	
	Examiner	Art Unit	
	Mojdeh Bahar	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5,6,14,15 and 19-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-6, 14-15, 19-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

- All species of EP4 receptor ligands and/or antagonists
- All species of a second therapeutic agent as recited in claim 21, e.g., COX-2 inhibitors, NSAIDS, 5-lipoxygenase inhibitors, leukotriene receptor antagonists, DMARDs, TNF receptor fusion proteins.

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

The claims are deemed to correspond to the species listed above in the following manner:

- 5, 6, 14-15, 19-29 are generic as to EP 4 receptor antagonist and

- 5, 6, 14-15, 1921, 24-26 and 28 are generic as to a second therapeutic agent

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: the EP4 ligands have many different structures and are not unified by any core. Furthermore the second therapeutic agents herein have many different structures and functions. The search for all possibilities and permutations of these species is a burden on the office. Note that the search is not limited to patent files.

During a telephone conversation with Lori Ann Morgan on 10 June 2003 a provisional election was made with traverse of compound species (I F) as the EP4 receptor ligand and COX-2 inhibitors as the second therapeutic agent. Affirmation of this election must be made by applicant in replying to this Office action.

Claims 5-6, 14-15, 19-29 are herein examined on the merits in so far as they read on the elected species of compound IF and the compounds disclosed in Foord et al. (GB2330307) and COX-2 inhibitors.

Claim Objections

Claim 21 is objected to because of the following informalities: parenthetical expressions "(COX-2)", "(NSAIDs)", "(DMARDs)", "(TNF)", "(NMDA)" are considered informal in the claim language. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-6, 14-15, 19-29 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for EP4 ligands and or antagonists represented on pages 3-8 of the specification, does not reasonably provide enablement for any and all EP4 ligands and/or antagonists. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art

7) the predictability of the art, and

8) the breadth of the claims.

Applicant fails to set forth the criteria that defines neither a "EP4 ligand" nor a "an EP4 antagonist". Additionally, Applicant fails to provide information allowing the skilled artisan to ascertain these compounds without undue experimentation. In the instant case, only a limited number of "EP4 antagonists", or "EP4 ligand" examples are set forth, thereby failing to provide sufficient working examples. It is noted that these examples are neither exhaustive, nor define the class of compounds required. The pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. The instant claims read on all "EP4 ligands" or "EP4 antagonist(s)", necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Note that there is no core structure among EP4 ligands and/or antagonists. Structurally they can be aminocyclopentane alkenoic acids as described in patent GB 2075503 A, a compound of formula IF, and oxazole compound as described in WO 00/18744 and 5-thio-ω-substituted phenyl prostaglandin E derivatives as described in WO 00/03980. Given the structural diversity among EP4 ligands, the Skilled Artisan would not be able to ascertain which compounds would be suitable for the practice of this invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 22-24 and 27-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Foord et al (GB2330307) in view of Katzung (Basic and Clinical Pharmacology, page 536-7, 1995).

Foord et al. (GB2330307) teaches compositions comprising EP4 antagonists. Foord also teaches that its compositions are useful in treating inflammatory bone disease, osteoarthritis and rheumatoid arthritis.

Foord et al. (GB2330307) does not teach the incorporation of COX-2 inhibitors in its composition.

Katzung teaches the employment of COX-2 inhibitors in treating inflammation including inflammatory arthritis.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ a COX-2 inhibitor in the composition of Foord et al. (GB2330307).

One of ordinary skill in the art would have been motivated to employ a COX-2 inhibitor in the composition of Foord et al. (GB2330307) because both EP4 antagonists and COX-2 inhibitors are known to be useful in treating inflammatory conditions and arthritis. Combining two agents which are known to be useful to treat arthritis and inflammation individually into a

single composition useful for the very same purpose is prima facie obvious. See *In re Kerkhoven* 205 USPQ 1069.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mojdeh Bahar whose telephone number is (703) 305-1007. The examiner can normally be reached on (703) 305-1007 from 8:30 a.m. to 6:30 p.m. Monday, Tuesday, Thursday and Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (703) 305-1877. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Mojdeh Bahar
Patent Examiner
September 30, 2003

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER

9/30/03